UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/066,895	02/04/2002	Keith Charles Deen	P50504C1	6077

7590 03/24/2004

GLAXOSMITHKLINE
Corporate Intellectual Property - UW2220
P.O. Box 1539
King of Prussia, PA 19406-0939

EXAMINER	
HELMS, LARRY RONALD	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 03/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/066,895	DEEN ET AL.	
	Examiner	Art Unit	
	Larry R. Helms	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *4-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 14-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/4/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of Group I, claims 1-3 and 14-17 in Paper mailed 2/6/04 is acknowledged.

2. Claims 4-13 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in Paper filed 2/6/04.

3. Claims 1-3 and 14-17 are under examination.

Specification

4. The disclosure is objected to because of the following informalities:

a. The first line of the specification should be updated to indicate that the instant application is a CON of 09/297344 which is abandoned.

b. The brief description of the drawings should indicate that figure 4 contains A-G and should be amended to recite "figures 4A-G illustrates".

Appropriate correction is required.

Claim Objections

5. Claims 2 and 17 are objected to because of the following informalities:

a. Claim 2 should indicate what SEQ ID Nos are referred to in the Figures.

b. Claim 17 recites "Hu19a" and should indicate "Hu19A".

c. Claim 2 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 1. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Appropriate correction is required.

Drawings

6. The drawings are objected to because Figure 4B recites SEQ ID NO:17 at the end of the nucleotide sequence but SEQ ID NO:17 is a 25 amino acid sequence.

Correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-3 and 14-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1-2 and 14-15 are indefinite for reciting "functional fragments thereof, specifically reactive with" in claim 1 because the exact meaning of the phrase is not

clear. It is not clear what function is being claimed for the "functional fragment" or how it is "specifically reactive" with an epitope. Does the phrase mean the "functional fragment" performs a chemical reaction with the F protein or does the phrase mean "specifically binds to"?

b. Claim 2 is indefinite because it is not clear if the claim is intending to depend on claim 1 and add additional light or heavy chains to the heavy or light chain claimed in claim 1 or claim the heavy and light chains of 19A, 19B, 19C, and 19D.

c. Claims 14-16 are indefinite for reciting "immunotherapeutically effective amount" in claims 14-15 because the exact meaning of the phrase is not clear. The phrase "effective amount" is indefinite when the claims fails to state the function which is to be achieve. In re Frederiksen, 213 F 2d 547, 102 USPQ 35 (CCPA 1954). Does the "effective amount" mean alleviating conditions, causing an immune response, etc?

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-3, 14-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a reshaped human monoclonal antibody and antigen binding fragments thereof which bind an epitope on the F protein of RSV and is

capable of neutralizing infection of the virus, wherein the antibody comprises a light chain of SEQ ID Nos 10, 11, and a heavy chain of SEQ ID Nos 5, 7, 6, or 8 and compositions comprising such antibodies, does not reasonably provide enablement for antibodies or fragments, which would not bind antigen, that do not contain a full set of all 6 CDRs from 3 CDRs from a light chain of SEQ ID Nos 10, 11, and 3 CDRs from a heavy chain of SEQ ID Nos 5, 6, 7, or 8, or any antibody with only a light chain constant region of SEQ ID Nos 12 or 13 with any heavy chain and pharmaceutical compositions comprising such. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are broadly drawn to antibodies or fragments that do not contain a full set of all 6 CDRs comprising 3 CDRs from a light chain of SEQ ID Nos 10, 11, and 3 CDRs from a heavy chain of SEQ ID Nos 5, 6, 7, or 8, wherein a partial set of CDRs would not bind antigen, or only a constant light chain of SEQ ID Nos 12 or 13 which would not bind antigen.

The specification teaches human monoclonal antibodies HU19A, HU19B, HU19C, and HU19D wherein the antibodies comprise a light chain of SEQ ID No 10, 11, and a heavy chain of SEQ ID Nos 5, 6, 7, or 8 and methods to detect RSV with such antibodies and compositions comprising such. The specification also teaches that the epitope region recognized by HU19A and HU19B is region 255-275 of the F protein (see page 40-41 Example G). The specification does not enable antibodies as broadly claimed. The specification does not teach an antibody of a light chain constant region of SEQ ID NO12 or 13 alone with a heavy chain.

The claims are not commensurate in scope with the enablement provided in the specification. The claims encompass antibodies which do not contain 3 CDRs from a light chain of SEQ ID Nos 10, 11, and 3 CDRs of the heavy chain from SEQ ID Nos 5, 6, 7, or 8 or a light chain alone and as such would not bind antigen.

It is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity which is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable

regions is required in order to form functional antigen binding sites. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proc Natl Acad Sci USA 1982 Vol 79 page 1979). Rudikoff et al. teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function. It is unlikely that antibodies as defined by the claims which may contain less than the full complement of CDRs from the heavy and light chain variable regions or have a light chain from one antibody and a heavy chain from any other antibody or have only a constant region defined have the required binding function. The specification provides no direction or guidance regarding how to produce antibodies as broadly defined by the claims. Undue experimentation would be required to produce the invention commensurate with the scope of the claims from the written disclosure alone.

Therefore, in view of the lack of guidance in the specification and in view of the discussion above one of skill in the art would be required to perform undue experimentation in order to practice the claimed invention.

11. Claim 17 is rejected under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention, because the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description.

It is unclear if a cell line which produces an antibody having the exact chemical identity of Hu19A, Hu19B, Hu19C, and Hu19D is known and publicly available, or can be reproducibly isolated without undue experimentation. Although the amino acid sequence of the light chain and heavy chain variable region and constant light chain regions are Shown in Figure 2 and 3, it is unclear if the entire amino acid sequence of the heavy chain hinge, CH1, CH2, CH3 regions are given. Therefore, a suitable deposit for patent purposes is suggested. Without a publicly available deposit of the above cell line, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of: (1) the claimed cell line; (2) a cell line which produces the chemically and functionally distinct antibody claimed; and/or (3) the claimed antibody's amino acid or nucleic acid sequence is an unpredictable event.

For example, very different V_H chains (about 50% homologous) can combine with the same V_K chain to produce antibody-binding sites with nearly the same size, shape, antigen specificity, and affinity. A similar phenomenon can also occur when different V_H sequences combine with different V_K sequences to produce antibodies with very similar properties. The results indicate that divergent variable region sequences, both in and out of the complementarity-determining regions, can be folded to form similar binding site contours, which result in similar immunochemical characteristics. [FUNDAMENTAL IMMUNOLOGY 242 (William E. Paul, M.D. ed., 3d ed. 1993)]. Therefore, it would require undue experimentation to reproduce the claimed antibody species Hu19A, Hu19B, Hu19C, and Hu19D. Deposit of the

hybridoma would satisfy the enablement requirements of 35 U.S.C. § 112, first paragraph. See, 37 C.F.R. 1.801-1.809.

Conclusion

12. No claims are allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (571) 272-0832. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached at (571) 272-0871.

14. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center telephone number is 703-872-9306.

Respectfully,

Larry R. Helms Ph.D.

571-272-0832